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EXAMINER	
SHIN, DANA H	

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1635	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/826,522	PLAETINCK ET AL.	
	Examiner	Art Unit	
	DANA SHIN	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 December 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *30,32-41,70-74 and 80-83* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *30,32-41,70-74 and 80-83* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on December 28, 2010 has been entered.

Status of Claims

Claims 30, 32-41, 70-74, and 80-83 are currently pending and under examination on the merits in the instant case.

Response to Arguments

Applicant's arguments with respect to claims 30-41, 70-74, and 80-83 rejected under 35 U.S.C. 103(a) over McAllister et al. filed with the RCE have been considered but are moot in view of the claim amendments and new ground(s) of rejection.

Note that the declaration under 37 CFR 1.132 filed on December 28, 2010 has been fully considered. However, the declaratory statements pertaining to the McAllister et al. reference are irrelevant to the currently amended claims because the DNA vector containing two opposing promoters of McAllister et al. requires two different promoters (one T3 promoter and a promoter

"other than" the T3 promoter), wherein the currently amended claims require two same promoters.

Claim Objections

Claims 37 and 70 are objected to because of the following informalities: The phrase "has been obtained" should be "is obtained" or "is". Appropriate correction is required.

Claim 80 is objected to under 37 CFR 1.75 as being a substantial duplicate of claim 36. Note that both claims are directed to a microorganism having two T7 promoters. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

All claims depending from claim 30 should refer to "The micro-organism according to claim 30" or variants thereof.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 30, 32-41, 70-74, and 80-83 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claims are drawn to a microorganism having a DNA vector comprising "a DNA sequence" that produces dsRNA. Note that claim 32 clarifies that the "DNA sequence" should be in a sense orientation as well as in an antisense orientation "relative to said promoters". That is, claim 32 requires that the DNA sequence must exist as two complementary DNA sequences or as having two distinct sequences: one as the DNA encoding the sense strand sequence and the other as the DNA encoding the antisense strand sequence. As such, the structural requirements claimed in the instant case are internally conflicting and inconsistent since a single DNA sequence cannot exist as two DNA sequences. Hence, one of ordinary skill in the art cannot ascertain the metes and bounds of the claimed subject matter, thereby rendering the claims indefinite. For examination purpose, the recitation of "a DNA sequence" will be interpreted to mean two complementary DNA sequences, one in a sense orientation and the other in an antisense orientation as recited in claim 32.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 30, 32-36, 39, 74, 80, and 83 are rejected under 35 U.S.C. 102(e) as being anticipated by Graham (US 6,573,099 B2, citation of record).

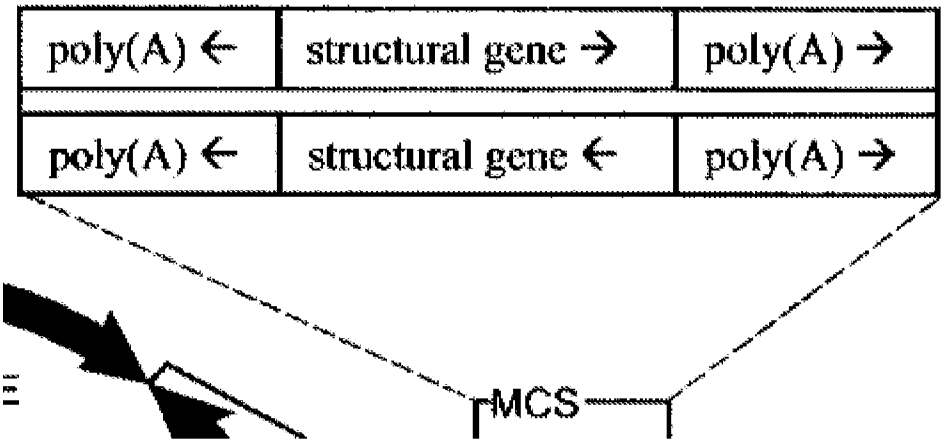
Graham discloses a cell comprising an isolated genetic construct "which is capable of delaying, repressing or otherwise reducing the expression of a target gene in an animal cell which is transfected with said genetic construct, wherein said genetic construct comprises at least two copies of a structural gene sequence and each copy of said structural gene sequence is separately placed under the control of a promoter which is operable in said cell, and wherein said structural gene sequence comprises a nucleotide sequence which is substantially identical to at least a region of said target gene, wherein at least one copy of said structural gene sequence is placed operably in the sense orientation under the control of an individual promoter sequence, and wherein at least one other copy of said structural gene sequence is placed operably in the antisense orientation under the control of another individual promoter sequence." See claim 4. Graham teaches that one can also introduce the isolated genetic construct into a plant cell or a yeast cell or a bacterial cell and transform the cell by utilizing promoters suitable for plant, yeast, and bacterial cells, for example, plant, yeast, and bacteria-derived promoters such as bacteriophage T7 promoter, bacteriophage T3 promoter, and SP6 promoter. See column 8, lines 4-25. Since the "isolated genetic construct" of Graham meets the structural requirements set forth for the "expression vector" claimed in the instant case, the yeast cell or bacterial cell comprising the isolated genetic construct of Graham would necessarily and inherently contain a double-stranded RNA produced by the isolated genetic construct that repress and reduces the target gene expression in the cell, absent evidence to the contrary. Note that when a rejection is based on a reference teaching a product appearing to be substantially identical to the claimed product, and

when the examiner presents reasoning tending to show inherency, the burden shift to the applicant to show an unobvious difference. See MPEP 2112: "[T]he PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his [or her] claimed product. Whether the rejection is based on inherency' under 35 U.S.C. 102, on prima facie obviousness' under 35 U.S.C. 103, jointly or alternatively, the burden of proof is the same...[footnote omitted]."

Response to Arguments

Applicant's arguments filed on December 28, 2010 have been fully considered but they are not persuasive. Applicant argues that the claims are not anticipated by Graham because Graham does not teach a "single sequence" between two promoters. As noted hereinabove in 35 U.S.C. 112, second paragraph rejections, the claims embrace a DNA sequence that exist as two complementary DNA sequences or as having two distinct sequences: one as the DNA encoding the sense strand sequence and the other as the DNA encoding the antisense strand sequence. As such, the genetic construct having the structural gene, wherein the gene comprises "one copy" in the sense orientation and "one other copy" in the antisense orientation, wherein the two copies are flanked and operably linked by two individual promoters as taught by Graham meets the structural requirements set forth in the instant claims, in light of the claim interpretation imparted by claim 32, hence encompassed by all pending claims in the instant case. See in particular claim 4 of Graham: "an animal cell which is transfected with said genetic construct, wherein said genetic construct comprises at least two copies of a structural gene sequence and each copy is separately placed under the control of a promoter which is operable in said cell, and wherein said

structural gene sequence comprises a nucleotide sequence which is substantially identical to at least a region of said target gene, wherein at least one copy of said structural gene sequence is placed operably in the sense orientation under the control of an individual promoter sequence, and wherein at least one other copy of said structural gene sequence is placed operably in the antisense orientation under the control of another individual promoter sequence." (emphasis added). See also Figure 21, which inherently depicts that the "sense orientation" structural gene and the "antisense orientation" structural gene are placed between the two individual promoter sequences, thus flanked by the promoters. See below:



See also column 20: "A multiple cloning site is positioned between the opposing CMV-IE and SV40 late promoter sequences in this plasmid" (emphasis added). Note that the multiple cloning site (MCS) depicted in Figure 21 contains the two copies of the structural gene in opposite orientations.

Hence, the disclosure of Graham as a whole teaches and suggests the instantly claimed subject matter. Accordingly, this rejection is hereby reiterated.

Claim 34 is rejected under 35 U.S.C. 102(a) as being anticipated by Timmons et al. (Nature, 1998, 395:854, applicant's citation).

See the priority denial as set forth in the Office action dated December 7, 2009 and as maintained in the Office action dated June 29, 2010.

Timmons et al. disclose a bacterial organism (bacterial strain BL21/DE3) comprising a DNA vector having two bidirectional T7 promoters flanking the DNA of interest, which is transcribed as a dsRNA in the bacterial organism. See Figure 1a. Hence, all limitations are taught by Timmons et al.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 30, 32-41, 70-74, and 80-83 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fire et al. (WO 99/32619, citation of record) in view of Graham (US 6,573,099 B2, citation of record), Ely et al. (US 5,837,848, citation of record), and Talkad et al. (Journal of Bacteriology, 1978, 135:528-541, citation of record).

Fire et al. teach that one can inhibit target gene expression in a cell with an expression vector that synthesizes and produces two separate complementary strands and form an RNA duplex inside the cell, wherein the cell is a plant cell, a yeast cell, or a nematode cell such as C. elegans cell. They teach that bacteriophage RNA polymerase promoters such as T3, T7, and SP6 promoters are useful for transcribing and synthesizing RNA. Note that the provisional application 60/068,562 filed on December 23, 1997 adequately supports the aforementioned teachings of Fire et al. See for examples claims 1, 14, 16, and 20 and pages 11 and 13. Fire et al. at the time of the priority filing date did not explicitly teach an expression vector comprising two opposing promoters, each of which transcribes and synthesizes each strand of a double-stranded RNA.

Graham discloses a cell comprising an isolated genetic construct "which is capable of delaying, repressing or otherwise reducing the expression of a target gene in an animal cell which is transfected with said genetic construct, wherein said genetic construct comprises at least two copies of a structural gene sequence and each copy of said structural gene sequence is separately placed under the control of a promoter which is operable in said cell, and wherein said structural gene sequence comprises a nucleotide sequence which is substantially identical to at least a region of said target gene, wherein at least one copy of said structural gene sequence is placed operably in the sense orientation under the control of an individual promoter sequence,

and wherein at least one other copy of said structural gene sequence is placed operably in the antisense orientation under the control of another individual promoter sequence." (emphasis added). See claim 4. Graham teaches that one can also introduce the isolated genetic construct into a plant cell or a yeast cell or a bacterial cell and transform the cell by utilizing promoters suitable for plant, yeast, and bacterial cells, for example, plant, yeast, and bacteria-derived promoters such as bacteriophage T7 promoter, bacteriophage T3 promoter, and SP6 promoter. See column 8, lines 4-25. Graham teaches that one can use two identical promoters or preferably use two different promoter sequences. See column 12, lines 42-50.

Ely et al. teach that one can use root-specific promoters to express a gene of interest in the roots of plants. They teach that the root-specific promoters are especially useful for expressing an insecticidal toxin to aid the plant roots to resist insect attack. See the entire reference.

Talkad et al. teach E. coli strains that are deficient in RNase III. They teach that RNase III cleaves bacteriophage T7 RNAs as well as double-stranded RNAs. See the entire reference.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use the two-promoter construction methodology of Graham to produce a double-stranded RNA in C. elegans, yeast, or RNase III-deficient E. coli.

One of ordinary skill in the art would have been motivated to do so with a reasonable expectation of success because use of a promoter-containing expression vector to transcribe and produce a double-stranded RNA was already known in the art as taught by Fire et al., and because using an expression vector containing a single promoter and using an expression vector containing two opposing promoters were alternative methodologies or approaches to produce

and express two separate copies of a gene of interest as taught by Graham. See and compare claims 3 and 4 of Graham. As such, an expression vector comprising a single promoter and an expression vector comprising two opposing promoters were art-recognized functional equivalents at the time the invention was made. Note that substituting art-recognized equivalents known for the same purpose is a well-established rationale in support of an obviousness rejection. See MPEP 2144.06. Further, since the industrial utility of a root-specific promoter-containing expression vector such that it can be used to express an insecticidal toxin to the root of a plant for protection of the root from insect attack was known in the art as taught by Ely et al., one of ordinary skill in the art wishing to produce a double-stranded RNA against an insecticidal toxin gene in a microorganism that can be applied to the root of a plant for protection against insect attack would have been motivated to make an expression vector comprising two opposing root-specific promoters and transform the selected microorganism with the expression vector. Further, since RNase III in bacteria was known to cleave and degrade baceteriophage T7 RNAs and double-stranded RNAs, it would have been apparent to a person of ordinary skill in the art to transform RNase III-deficient E. coli bacteria with the dual promoter system in order to allow the system to efficiently produce the double-stranded RNA product that remains preserved in the cells of E. coli bacteria. Since all skills, knowledge, and methodologies to arrive at the claimed invention were known in the art at the time the invention was made, the claimed invention taken as a whole would have been prima facie obvious at the time of filing.

Response to Arguments

Applicant's arguments filed on December 28, 2010 have been fully considered but they are not persuasive. Applicant argues that the claims are not obvious in view of the declaration of Dr. Sablon filed on December 28, 2010. Since applicant's entire arguments refer to the declaration, the declaration will be discussed for maintaining and reiterating this rejection in the instant Office action.

The declaration under 37 CFR 1.132 filed on December 28, 2010 is insufficient to overcome the rejection of the claims as set forth in the last Office action because of the following reasons:

The declarant states that the claims are not obvious because 60/068,562 does not disclose "simultaneous" synthesis of two RNA strands in a bacterium using two promoters. See paragraph 18. Applicant's attention is directed to the fact that one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See In re Keller, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); In re Merck & Co., 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). Note that this rejection is not established solely on the Fire et al. reference. Also note that the instant rejection is an obviousness rejection, not an anticipation rejection. As such, a single reference is not required to disclose all the limitations claimed instant case.

The declarant goes on to discuss the cited prior art references in 60/068,562 and states that the vector construction references described on page 11 of 60/068,562 are "standard laboratory manuals.", which do not teach producing two RNA strands. The declarant further states that the vectors described in 60/068,562 require two plasmids, each of which produces

single-stranded RNA. See paragraphs 19-20. Again, note that one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references, wherein the Fire et al. reference is not the only reference cited in the instant obviousness rejection. In addition, contrary to the declarant's statement that Fire et al. taught only two plasmids producing two strands, Fire et al. explicitly taught that one can either chemically synthesize double-stranded RNA molecules or transcribe double-stranded RNAs inside a cell by using a vector that synthesizes double-stranded RNA molecules. See page 7: "RNA may be synthesized either in vivo or in vitro. Endogenous RNA polymerase of the cell may mediate transcription in vivo, or cloned RNA polymerase can be used for transcription in vivo or in vitro. For transcription from a transgene in vivo or an expression vector, a regulatory region (e.g., promoter, enhancer, silencer) is used to transcribe the RNA strand(s)." (emphasis added). They also taught that the regulatory promoter can be "a bacteriophage RNA polymerase (e.g., T3, T7, SP6)." See page 11. See also claim 20, which is directed to a "method to inhibit expression of a target gene in a cell comprising introduction of a ribonucleic acid (RNA) into the cell in an amount sufficient to inhibit expression of the target gene, wherein the RNA has a double-stranded structure" (see claim 1; emphasis added), wherein "an expression vector in a cell produces the RNA." (see claim 20; emphasis added). Hence, the disclosure of 60/068,562 clearly suggests transcribing both RNA strands simultaneously from an expression vector having a bacteriophage RNA polymerase promoter such as T3, T7, or SP6. In addition, Fire et al. also taught the utility of tissue-specific promoter (e.g., myo-3 promoter; see page 16). Again, note that the instant obviousness rejection is not solely based on the teachings and suggestions of Fire et al. but further in combination with Graham, who taught using two opposing promoters to

synthesize/transcribe two RNA strands. Again, the vector construction methodology of Graham may not be disclosed on page 11 of 60/068,562; however, the methodology of Graham was an art-recognized methodology for producing two RNA strands in a simultaneous manner by using two opposing, bi-directional promoters (one in the sense orientation, and the other in the antisense orientation), wherein such methodology was utilized in the art prior to the earliest filing date sought by applicant.

The declarant has merely stated that one skilled in the art would not have expected to practice the claimed invention "based on the cited combinations of prior art references", without providing a clear articulation as to why or how the combined teachings of the cited prior art references would have not guided a person of ordinary skill in the art to make a microorganism having an expression vector that produces a double-stranded RNA in a cell of the microorganism, wherein the vector contains two opposing promoters, each of which transcribes a sense RNA strand and an antisense RNA strand.

It is noted that applicant has argued that "Graham does not provide an element of the claimed invention." because the claims require "only one structural gene sequence", whereas the vector structure of Graham requires two sequences. Contrary to applicant's argument, as stated hereinabove (see the 112, second paragraph rejection and the 102(e) rejection), the instant claims do require two DNA sequences "in a sense and an antisense orientation relative to said promoters". See claim 32. In addition, see the reasons for maintaining and reiterating the 102(e) rejection hereinabove.

In view of the foregoing, since neither applicant's arguments nor the declarant's statements are found persuasive, this rejection is reiterated herein.

Claims 30, 32-41, 70-74, and 80-83 are rejected under 35 U.S.C. 103(a) as being unpatentable over Montgomery et al. (TIG, 1998, 14:255-258, applicant's citation) in view of Studier et al. (Methods in Enzymology, 1990, 185:60-89), Timmons et al. (East Coast Worm Meeting Abstract 180, May 12, 1998, applicant's citation), Vanfleteren et al. (Experientia, 1976, 32:1087-1088, applicant's citation), Williamson et al. (Plant Cell, 1996, 8:1735-1745, applicant's citation), Ely et al. (US 5,837,848, citation of record), and Talkad et al. (Journal of Bacteriology, 1978, 135:528-541, citation of record).

Note that this rejection is established on the applicant's imposed claim interpretation that the promoters flank one single-stranded DNA sequence. See applicant's remarks filed on December 28, 2010.

Montgomery et al. teach that a dsRNA can be transcribed/produced in a cell from a "single" gene "sequence", wherein a sense transcript and an antisense transcript are "simultaneously" transcribed/produced by an operably linked "promoter" (e.g., T7) that synthesizes the sense transcript and by a "cryptic transcription start site" or "spurious internal initiation" that synthesizes the antisense transcript, wherein the sense transcript and the antisense transcript (or sense and antisense RNA "preparations") undergo intramolecular "hybridization" to produce a double-stranded RNA (dsRNA), which is capable of RNA interference. Figure 1.

Studier et al. teach a bacterial (E. coli) host cell organism a bacterial organism (bacterial strain BL21/DE3) having a plasmid vector with an "antisense promoter", which synthesizes "antisense RNA after T7 RNA polymerase has been induced." See page 88. They also show bacterial cells expressing target (sense) RNA transcripts from a T7 promoter in a sense orientation. See Figure 1.

Timmons et al. report that C. elegans can be fed with bacteria that express dsRNA, wherein the dsRNA is expressed from a muscle tissue-specific promoter myo3. See the entire abstract.

Vanfleteren teaches that yeast extract is an inexpensive food source for C. elegans and that it can be fed to C. elegans on a large scale. See the entire reference.

Williamson et al. teach that plant parasitic nematodes such as root-knot nematodes infect plant roots. Hence, they teach that nematodes feed on plant cells, especially root cells. See the entire reference.

Ely et al. teach that one can use root-specific promoters to express a gene of interest in the roots of plants. They teach that the root-specific promoters are especially useful for expressing an insecticidal toxin to aid the plant roots to resist insect attack. See the entire reference.

Talkad et al. teach E. coli strains that are deficient in RNase III. They teach that RNase III cleaves bacteriophage T7 RNAs as well as double-stranded RNAs. See the entire reference.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to make and use a DNA vector comprising two same non-cryptic, non-spurious promoters (e.g., T7 or tissue-specific or root-specific promoters) that are oppositely oriented, wherein the promoters flank a single DNA sequence that is transcribed to produce RNA transcripts that are oppositely oriented, wherein the RNA transcripts form dsRNA when the DNA vector is present in an E. coli or yeast cell.

One of ordinary skill in the art would have been motivated to do so with a reasonable expectation of success because the mechanism whereby an RNAi-mediating dsRNA molecule is

produced from a DNA construct containing only a DNA sequence having only a sense orientation promoter was proposed by Montgomery et al. such that a "cryptic" or "spurious" promoter-like transcription initiation structure in an antisense orientation produces antisense-oriented RNA transcripts from a DNA sequence, whereas a distinct sense-oriented promoter (e.g., T7) produces sense-oriented RNA transcripts from a DNA sequence, wherein the antisense-oriented RNA transcripts and the sense-oriented RNA transcripts form double-stranded RNAs by intramolecular hybridization, wherein Montgomery et al. suggested that the amount/number of the antisense-oriented RNA transcripts produced by the "cryptic" or "spurious" promoter-like transcription initiation structure in the antisense orientation is far less than the sense-oriented RNA transcripts produced by the distinct promoter structure (e.g., T7). As such, in light of the mode of action whereby a DNA vector structure is able to produce dsRNAs inside a cell as illustrated in Figure 1 of Montgomery et al., and further in view of the fact that the cryptic" or "spurious" promoter-like transcription initiation structure is not as effective as a distinct promoter structure (e.g., T7) in producing RNA transcripts, thereby the number/amount of dsRNAs formed inside a cell is not equivalent to the number/amount of sense-oriented RNA transcripts produced by the distinct promoter structure, a person of ordinary skill in the art would have been motivated to introduce a non-cryptic, non-spurious, distinct promoter structure (e.g., T7) in an antisense orientation such that antisense RNA transcripts are as effectively synthesized as sense RNA transcripts, thereby equimolar sense and antisense RNA transcripts are produced, thereby increasing the number/amount of dsRNAs when compared to the DNA vector shown in Figure 1 of Montgomery et al.

Note that synthesizing antisense RNA transcripts using a T7 promoter in an antisense orientation has long been known to be feasible as taught by Studier et al., and the scientific concept that one can simultaneously produce two oppositely oriented RNA transcripts from a single DNA sequence, wherein the RNA transcripts form a duplex RNA structure capable of inducing RNA in a cell was suggested in the art as taught by Montgomery et al.

In addition, note that RNase III was known to cleave and degrade bacteriophage T7 RNAs as well as double-stranded RNAs and the methodologies for making RNase III-deficient E. coli strain were known in the art as taught by Talkad et al., wherein one of ordinary skill in the art would have been motivated to make an RNase III-deficient E. coli strain having a DNA vector with two opposing T7 promoters that flank a C. elegans-specific target DNA sequence and use it as the food source to express dsRNA in C. elegans since feeding dsRNA-expressing bacteria to C. elegans was demonstrated by Timmons et al. Moreover, one would have been motivated to make a yeast cell that expresses a a DNA vector with two opposing T7 promoters that flank a C. elegans-specific target DNA sequence and use it as the food source to express dsRNA in C. elegans since yeast cells were art-recognized inexpensive food source for C. elegans as taught by Vanfleteren.

Further, one would have been motivated to use two opposing root-specific promoters that flank a root-knot nematode-specific DNA sequence that is essential for the survival or biological activity of the parasitic root-knot nematode, thereby making an RNase III-deficient E. coli cell or a yeast cell containing dsRNA targeted to the root-knot nematode-specific DNA sequence, hence using the anti-root-knot nematode dsRNA-containing cell as an insecticidal composition for plants such that root-knot nematodes feeding on the root cells of plants that are exposed to the

dsRNA-containing cell (bacteria or yeast) would ingest the cell having the insecticidal composition thus would no longer be able to infect and feed on the plant roots, because plant parasitic nematodes such as root-knot nematodes were known to infect and feed on plant roots as taught by Williamson et al., and because using plant root-specific promoters to express an insecticidal toxin in the roots of plants was an art-accepted methodology as taught by Ely et al., and because making and using target-specific dsRNAs that suppress target activity in nematodes were known in the art as taught by Montgomery et al. and Timmons et al.

In view of the foregoing, the claims taken as a whole would have been prima facie obvious even if applicant's imposed claim interpretation is utilized.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., In re Berg, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); In re Goodman, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); In re Longi, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); In re Van Ornum, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); In re

Vogel, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and In re Thorington, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 30, 32-41, 70-74, and 80-83 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 26-27 of U.S. Patent No. 7,358,069 B2. Although the conflicting claims are not identical, they are not patentably distinct from each other because both the instant claims and the reference claims are drawn to a bacterial cell of E. coli comprising a DNA construct producing a double-stranded RNA, wherein the construct comprises two promoters. Although the reference claims do not explicitly recite that T3, T7, SP6, wherein the bacterial cell is RNase III-deficient strain, the specification of the U.S. Patent teaches the limitations. See columns 3 and 10. The specification also teaches that one can express dsRNA obtained from C. elegans. See column 10. As such, the scope of the instant claims and that of the reference claims overlap with each other.

Response to Arguments

Applicant's arguments filed on December 28, 2010 have been fully considered but they are not persuasive. Applicant argues that the examiner failed to provide "a sound basis" for the obviousness of the instant claims over claims 26-27 of U.S. 7,358,069 B2. Contrary to applicant's argument, the examiner has explicitly provided "a sound basis" for the obviousness of the instant claims over the reference claims. See pages 12-13 of the last Office action. Note that the instant specification explicitly teaches that the expression vector comprises a stop signal sequence. Note that applicant has stated that the reference claims "require" the presence of a transcription terminator. Note that the instant claims as currently written do not exclude the presence of a transcription terminator but instead the claims embrace a vector having a transcription terminator as evidenced by the open-ended "comprising" language in the claims as well as the explicit disclosure of the instant specification that contemplates using transcription terminator sequences. See paragraph 0020: "Preferably, according to this embodiment the nucleotide sequence comprises stop codons sufficient to prevent translation of the nucleotide sequence following integration into said chromosome." (emphasis added). See also paragraph 0089: "An E. coli vector can be constructed harboring the following features; Two T7 promoters directed towards each other, with a restriction site or a multiple cloning site in between. Furthermore, the vector may contain the C. elegans sup-35 genomic DNA, engineered in such a way that it contains several stop codons at various intervals" (emphasis added). Again, a transcription terminator is not excluded from the vector claimed in the instant case, and moreover, in view of the teachings of the instant specification (see paragraphs 0020 and 0089), making a microorganism having a vector having two T7 promoters and a transcription terminator

as claimed in U.S. 7,358,069 B2 would have been obvious. As such, the invention defined in the instant case is an obvious variation and overlaps in scope with the invention defined in U.S. 7,358,069 B2.

Applicant has further asserted that the instant claims are patentably distinguished from U.S. 7,358,069 B2 because claims 26-27 of U.S. 7,358,069 B2 do not "recite" features that are "recited" in the instant claims. First, applicant's attention is directed to the fact that the instant rejection is not a double patenting rejection under 35 U.S.C. 101, wherein the claims at issue are rejected as claiming the identical subject matter claimed in an issued U.S. patent. Second, applicant's attention is directed to the fact that the instant rejection is an obviousness double patenting rejection, wherein the instant rejections are determined to be obvious over the reference claims of U.S. 7,358,069 B2. Now, as such, the mere fact that certain "features" are not "recited" word for word between the instant claims and the reference claims does not render the instant claims nonobvious over the reference claims. Note that the reference claims do require two promoters "in opposite orientation" as required in the instant claims. Further, note that the reference claims are drawn to a microorganism harboring a DNA construct that "produces double stranded RNA" as required in the instant claims. Further, it is prima facie obvious that the DNA sequence claimed in U.S. 7,358,069 B2 that is transcribed as double stranded RNA is positioned between the two promoters. See Figure 1b of U.S. 7,358,069 B2, for example. See also Figure 3 of U.S. 7,358,069 B2 having two identical T7 promoters as claimed in the instant case. Hence, the claimed subject matter in the instant case is encompassed by the reference claims such that the scope of the claims in the instant case and U.S. 7,358,069 B2 overlap with each other. Again, this rejection is an obviousness rejection, not a 35 U.S.C. 101 rejection.

Since applicant's arguments are not persuasive, and since applicant has not provided a signed terminal disclaimer to overcome this rejection, this rejection is hereby reiterated.

Claims 30, 32-41, 70-74, and 80-83 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 34-39 U.S. Patent No. 7,932,062. Although the conflicting claims are not identical, they are not patentably distinct from each other because both the instant claims and the reference claims are drawn to a bacterial cell of E. coli comprising a DNA construct producing a double-stranded RNA, wherein the construct comprises two promoters. Although the reference claims do not explicitly recite that T3, T7, SP6, wherein the bacterial cell is RNase III-deficient strain, the specification of the copending application teaches the limitations. The specification also teaches that one can express dsRNA obtained from C. elegans.. As such, the scope of the instant claims and that of the reference claims overlap with each other.

Response to Arguments

Applicant's arguments filed on December 28, 2010 have been fully considered but they are not persuasive. Applicant argues that since claims 34-39 of 12/055,607 are not allowable, applicant defers addressing this rejection. Applicant's attention is directed to the fact that 12/055,607 is now patented as U.S. Patent No. 7,932,062. Since applicant's arguments are not persuasive, this rejection is hereby reiterated.

Claims 30, 32-41, 70-74, and 80-83 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 24-25 of copending Application No. 11/666,017. Although the conflicting claims are not identical, they are not patentably distinct from each other because both the instant claims and the reference claims are drawn to a cell (E. coli bacterial cell or a yeast cell or a nematode cell) comprising a double-stranded RNA. Although the reference claims do not explicitly recite that the double-stranded RNA is produced from a vector comprising two promoters, the specification of the copending application teaches that one can use such vector for producing double-stranded RNA in a cell, wherein the promoters are selected from T7, SP6 and root-specific promoters. See pages 39-44. As such, the scope of the instant claims and that of the reference claims overlap with each other.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Response to Arguments

Applicant's arguments filed on December 28, 2010 have been fully considered but they are not persuasive. Applicant has merely stated that since 11/666,017 is not allowable, applicant defers addressing this rejection. Since applicant has not provided any rebuttal arguments or a signed terminal disclaimer, this rejection is hereby reiterated.

Claims 30, 32-41, 70-74, and 80-83 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 27-28 and 34-

35 of copending Application No. 11/666,021. Although the conflicting claims are not identical, they are not patentably distinct from each other because both the instant claims and the reference claims are drawn to a cell (E. coli bacterial cell or a yeast cell) comprising a double-stranded RNA. Although the reference claims do not explicitly recite that the double-stranded RNA is produced from a vector comprising two promoters, the specification of the copending application teaches that one can use such vector for producing double-stranded RNA in a cell, wherein the promoters are selected from T7, SP6 and root-specific promoters. See pages 1, 18-19, 30-32. As such, the scope of the instant claims and that of the reference claims overlap with each other.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Response to Arguments

Applicant's arguments filed on December 28, 2010 have been fully considered but they are not persuasive. Applicant has merely stated that since 11/666,021 is not allowable, applicant defers addressing this rejection. Since applicant has not provided any rebuttal arguments or a signed terminal disclaimer, this rejection is hereby reiterated.

Claims 30, 32-41, 70-74, and 80-83 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 44 of copending Application No. 11/992,090. Although the conflicting claims are not identical, they are not patentably distinct from each other because both the instant claims and the reference claims are drawn to a cell comprising a double-stranded RNA. Although the reference claims do

not explicitly recite that the double-stranded RNA is produced from a vector comprising two promoters the specification of the copending application teaches that one can use such vector for producing double-stranded RNA in a cell, wherein the promoters are two identical promoters (e.g., tissue-specific promoters, T7, T3, SP6), wherein the bacterial cell is RNase III-deficient strain. The specification also teaches that one can express dsRNA obtained from C. elegans. In fact, the specificity teaches making and using a vector with "two identical T7 promoters" for producing a double-stranded RNA. See paragraphs 0106, 0168, 0239. As such, the scope of the instant claims and that of the reference claims overlap with each other.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 30, 32-41, 70-74, and 80-83 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 21-22 of copending Application No. 11/992,091. Although the conflicting claims are not identical, they are not patentably distinct from each other because both the instant claims and the reference claims are drawn to a cell (bacterial cell or a yeast cell) comprising a double-stranded RNA. Although the reference claims do not explicitly recite that the double-stranded RNA is produced from a vector comprising two promoters, the specification of the copending application teaches that one can use such vector for producing double-stranded RNA in a cell, wherein the promoters are two identical promoters, wherein the bacterial cell is RNase III-deficient strain. The specification also teaches that one can express dsRNA obtained from C. elegans. In fact, the specificity teaches making and using a vector with "two identical T7 promoters" for producing a

double-stranded RNA. See paragraph 0219. As such, the scope of the instant claims and that of the reference claims overlap with each other.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 30, 32-41, 70-74, and 80-83 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 4 of copending Application No. 12/087,536. Although the conflicting claims are not identical, they are not patentably distinct from each other because both the instant claims and the reference claims are drawn to a cell comprising a double-stranded RNA. Although the reference claims do not explicitly recite that the double-stranded RNA is produced from a vector comprising two promoters, the specification of the copending application teaches that one can use such vector for producing double-stranded RNA in a cell, wherein the promoters are two identical promoters (e.g., tissue-specific promoters, T7, SP6), wherein the bacterial cell is RNase III-deficient strain. The specification also teaches that one can express dsRNA obtained from C. elegans. In fact, the specificity teaches making and using a vector with "two identical T7 promoters" for producing a double-stranded RNA. See paragraphs 166, 0170, 0204. As such, the scope of the instant claims and that of the reference claims overlap with each other.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 30, 32-41, 70-74, and 80-83 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 6-12 and 40 of copending Application No. 12/087,537. Although the conflicting claims are not identical, they are not patentably distinct from each other because both the instant claims and the reference claims are drawn to a cell (bacterial cell or a yeast cell) comprising a double-stranded RNA. Although the reference claims do not explicitly recite that the double-stranded RNA is produced from a vector comprising two promoters, the specification of the copending application teaches that one can use such vector for producing double-stranded RNA in a cell, wherein the promoters are selected from T3, T7, SP6, wherein the bacterial cell is RNase III-deficient strain. See pages 30-31, 48. The specification also teaches that one can express dsRNA obtained from C. elegans. See page 17. As such, the scope of the instant claims and that of the reference claims overlap with each other.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Response to Arguments

Applicant's arguments filed on December 28, 2010 have been fully considered but they are not persuasive. Applicant has merely stated that since 12/087,537 is not allowable, applicant defers addressing this rejection. Since applicant has not provided any rebuttal arguments or a signed terminal disclaimer, this rejection is hereby reiterated.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to DANA SHIN whose telephone number is (571)272-8008. The examiner can normally be reached on Monday through Friday, 7am-3:30pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Heather Calamita can be reached on 571-272-2876. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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